DISCUSSION

A revolution came in the field of peripheral nerve blocks after the introduction of BPB as it has decreased the need forgeneral anesthesia (GA) and the complications associated with it. BPB was first performed by Halsted in 1884, and then Crile in 1887.[79] The present systematic review was conducted to compare the complications of the 73 RCTs that have used any of the techniques for blocking brachial plexus.

One of the advances in the field of regional anesthesia was the introduction of US which is considered as the "gold standard" of regional anesthesia. The first report about the application of the US was published in 1989 by Ting and Sivagnanratnam.[80] The US-guidance predicts a more accurate and efficient deposition of LA due to the visibility of the neural targets, the vascular structures, and the spread of LA.[81] In our systematic review, most of the studies (n=38) have utilized the US for increasing the efficiency of the block procedure. Renes SH et al,[21] Thomas LC et al,[27] and Ghodki and Singh,[48] found higher success rate with the US-guided ISBPB group (100% vs 95% vs 100%) as compared to NS-ISBPB group (93% vs 91% vs 99%) respectively. Renes SH et al,[21] and Ayyanagouda B et al,[65] concluded that US-guided ISBPB reduces the incidence of HDP. Liu GY et al,[41] and Karaman T et al,[63] found that US-guidance reduces the risk of pneumothorax, is feasible, and almost has no complications. Yuan Ja-Min in their systematic review concluded that blocks performed using US guidance were more likely to be successful (risk ratio (RR) for block success 0.36, 95% CI 0.23–0.56, P <0.00001), decreased incidence of vascular puncture during block performance (RR 0.13, 95% CI 0.06–0.27, P <0.00001), decreased the risk of complete hemi-diaphragmatic paresis (RR 0.09, 95% CI 0.03–0.52, P=0.0001).[1]

In the present systematic review, a total of 30 studies,[6,7,8,10,12,13,16,19,21,24,29,30,32,33,34,36,35,36,37,38,41,42,43,44,49,50,53,68,69,70,72,78] have used the single-injection technique of LA. There has been controversy regarding the technique of LA injection as some authors were in favor that the success rate of multiple injections was better than the single-injection technique in blocking the brachial plexus. Even, the duration of anesthesia was rapid in multiple injections rapidly than one injection.[82,83,84] Park SK et al in their systematic review found that multiple injection technique may be better based on the analysis of the spread of peripheral nerve block,[85] but another systematic review conducted by Albrecht et al concluded that single injection is better than multiple injections as it takes less time and causes less paraesthesia,[86] whereas, four studies,[10,11,19,35] included in our systematic review found that both injection techniques have equivalent effects. Refaat S et al found that the intracluster technique for SBPB showed rapid onset with adequate postoperative analgesia and minimal complications as compared to single and double injection techniques.[71]

In the present systematic review, many studies have used adjuvants such as clonidine,[70] MgSO4,[62,66,68] fentanyl,[56,60,77] dexamethasone,[25,54,76,78] and dexmedetomidine,[55,56,59-62,70,75,76,77] to LA to prolong the duration of block. Parrington SJ et al,[25] and Youssef MY et al,[78]found that the addition of dexamethasone to LA prolongs the duration of analgesia and respective blocks. Kaur S et al,[66] and Elhusein AKA et al,[68] stated that the addition of MgSO4 has a lesser incidence of side effects and also decreases the analgesic requirements. When dexmedetomidine added with LA, all the studies,[55,56,59,60,61,62,70,75,76,77] found that the adjuvant prolongs the duration of sensory and motor blocks, as well as the duration of postoperative analgesia. Similar findings were found by various studies conducted in the past.[87,88,89] Dexmedetomidine is an α2 agonist and a newer congener of clonidine but in our review, almost all the studies,[55,56,59-62,75,76,77] except Singh and Singham,[70] found hypotension and bradycardia as the complication when dexmedetomidine was

added as an adjunct to LA.

Complications associated with BPB

Although BPB is the most common block used for upper limb surgery, it is not free from complications. These complications can be devastating for the patients as well as for the performing anesthesiologist. We found that the most common complication found among most of the studies was neurological (n=41) followed by respiratory (n=23) and cardiac complications (n=13).

(1) Neurological complications

We found that more than half of the studies (n=41) reported neurological complications. During surgery, nerves are sometimes injured causing neurological complications. These complications are well-recognized since the early days. Most of the neurological complications resolve on its own without any treatment. Serious permanent nerve injury following the block is very rare.[3] The most common neurological complication found in our systematic review is Horner syndrome (n=32) followed by paresthesia (n=21) and tingling/numbness (n=4). The detailed elaboration of these complications along with their studies are:

(a) Horner syndrome: It is a neurologic condition consisting of a triad of miosis, ptosis, and anhidrosis. The sympathetic outflow to the ipsilateral head and neck is interrupted due to the spread of the LA to the prevertebral spaces causing Horner syndrome.[90] The incidence of Horner syndrome following the ISBPB technique ranges from 20% to 90%. Despite using the same approach and same LA regimen, the incidence of Horner syndrome varies between the studies,[90,91] which may be due to the mal-distribution of LA in the brachial plexus sheath.[92]

A total of 32 studies,[7,10,12,14,16,19,20,21,23,24,33,35,36,40,42,44,45,46,47,48,50,57,58,61,63,65,67,69,70,71,73,74] have depicted the incidence of Horner syndrome. Among them, 18 studies compared two or three techniques of BPB

and the rest (n=14) have focused on only one approach of BPB. Six studies,[14,16,33,44,48,65] that reported the complications of Horner syndrome were related to the ISBPB technique alone. These studies were conducted by Riazi S et al,[16] (lower incidence of Horner syndrome with low-volume LA (5ml) as compared to the high volume (20ml), Kaya M et al,[33] (more with single-injection technique), Ghodki and Singh,[48] (more with the NS group as compared to the US group), Palhais A et al,[44] and Ayyanagouda B et al.[65] Palhais A et al,[44] and Ayyanagouda B et al,[65] found a lesser incidence of Horner syndrome with extrafascial group (20% and 20.7%) as compared to the intrafascial group (35% and 27.6%) respectively. Six studies have reported the complication of Horner syndrome in studies related to the SBPB technique. These six studies are: Renes SH et al,[21] Arab SA et al,[35] (more with triple injection technique as compared with single-injection technique), Kooloth RA et al,[42] (more with the group using bupivacaine as compared to ropivacaine), Mangal V et al,[61] (more incidence with dexmedetomidine group), Singh and Singham,[70] (more incidence with the Dexmedetomidine group as compared to clonidine group), and Refaat S et al.[71] Horner syndrome was reported in the IBPB technique only in two studies conducted by Tran DQH et al,[19](more with single-injection technique) and Kasine T et al.[73] A systematic review conducted by Schubert AK et al found that the SBPB had a significantly lower incidence of Horner's syndrome than the ISBPB (7.57% versus 28.20%).[93] This agrees with the findings of our systematic review also. Seven studies have compared the ISBPB and SBPB techniques of which, six of them (Ryu T et al,[40] Wiesmann T et al,[46] Koh WU et al,[47] Aliste J et al,[57] Karaman Tet al,[63] and Singh and Singham,[69] found higher incidence with ISBPB and only one showed higher incidence in SBPB.[50] A systematic review done by Park SK et al compared the US-guided SBPB and IBPB found a greater incidence of Horner syndrome with US-guided SBPB (32.1%) as compared to US-guided IBPB.[85]Even in our systematic review,when the SBPB technique was compared with IBPB in

three studies,[20,24,36] all of the studies found a higher incidence of Horner syndrome with SBPB as compared to IBPB. In three of the studies, IBPB was compared with AXB. Out of which, two studies,[7,10] have shown a greater incidence of Horner syndrome with IBPB but the third study,[12] has showna higher incidence with the AXB. In two studies,[23,45] SBPB, IBPB, and AXB were compared, both of them found higher incidence with SBPB, whereas, Auyong DB et al compared ISBPB, SBPB, and suprascapular and found higher incidence with ISBPB.[58] Blanco AFG et al have compared IBPB and RBPB and found equal incidence in both studies.[67] The Cochrane systematic review compared the risk of Horner syndrome with IBPB and other techniques and found that other techniques have 12.1% chances of Horner syndrome as compared to IBPB (2.2%) and the difference between them is also significant ($p<0.0001$).[2] A study conducted by Neal JM et al reported that the incidence of Horner syndrome in SBPB technique can be reduced to 90% with the use of US as it reduces the requirement of LA due to exact positioning of the needle around the nerve which in turn reduces the escape of the LA towards the paravertebral spaces, hence reduces the incidence of Horner syndrome.[91] The study of the SBPB technique included in our review also agrees with this point and found a greater incidence with NS-SBPB as compared to US-SBPB.[22] However, Luo Q et al found a higher incidence with US-guided SBPB as compared to US-guided CBPB ($p <0.01$).[74] Stasiowski M et al assessed the development of Horner syndrome after ISBPB found a significantly higher incidence in younger patients.[90] However, we have not included studies conducted in patients less than 18 years of age.

(b) Paresthesia: It refers to the persistent anesthesia that extends even after the expected duration of anesthesia. It manifests as a burning or prickling sensation in the hands, legs, or any part of the body. Paresthesia can happen after the administration of a peripheral nerve block such as the BPB. The incidence of transient paraesthesia can be as high as

8–10% after the BPB.[11]

We found that a total of 21 studies,[8,9,10,11,13,15,17,19,20,23,26,27,32,36,44,52,54,57,65,67,72]have reported paresthesia as their complication. Of these 21 studies, seven studies were based on the comparison of the two techniques, and the rest (n=14) are based on individual techniques. Six studies,[8,9,11,15,26,32] were conducted on the AXB technique and reported this complication. These were conducted by Serradell A et al,[8] (more incidence of paresthesia/dysesthesia with 20ml LA group followed by 36 ml and 28ml), March X et al,[9] Liu FC et al,[11] (more incidence in nerve stimulator-guided and the double-injection group as compared to US-guided double and single-injection groups, p=0.03), Chan VWS et al,[15] (13patients in both Groups US and NS and nine in Group USNS AXB techniques, Gianesello L et al,[26] (equal incidence with electrical nerve stimulation and fascial pop technique of AXB), and Bernucc F et al,[32] (more incidence with perineural AXB as compared to perivascular AXB). Four studies,[17,19,52,54] have reported paraesthesia with the IBPB technique. A systematic review done by Albrecht E et al,[86] concluded that the rate of procedural paraesthesia was less with one injection than multiple injections, relative risk (95% CI) 0.6 (0.4–0.9), p = 0.004, whereas, Tran DQH et al,[19] found equal incidence with single and double injection techniques with IBPB. Four studies,[27,44,65,72] have reported the incidence with the ISBPB technique. Palhais A et al (0 vs 30%),[44] and Ayyanagouda B et al,[65] (0% vs 31%) have compared the extrafascial and intrafascial approaches respectively and were in favor that the extrafascial injection reduces the incidence of paresthesia. Seven studies have compared the two techniques of BPB.

The findings of a systematic review conducted by Park SK et al,[85] concluded that procedure-related paresthesia and adjacent nerve-related complications were more frequent in SBPB as compared to IBPB. Another systematic review conducted by Albrecht et al,[86] also found that paraesthesia

was less common with the IBPB approach as compared to the SBPB approach. Two studies,[20,36] in our systematic review have compared the SBPB with the IBPB technique and found a greater incidence with the SBPB technique in both studies. Yazer MS,[36] et al also found a greater incidence with the SBPB (18.7%) as compared to the IBPB (3.1%). Even, Koscielniak-Nielsen JZ et al,[20] have found a statistically significant greater incidence with the SBPB as compared to the IBPB (P=0.003).

Aliste J et al,[57] found a greater incidence with the ISBPB technique as compared to the SBPB. When the AXB was compared with the IBPB in the Rettig HC study,[10]a greater incidence of paresthesia was seen with IBPB. Soeding PF et al,[13] compared ISBPB and AXB and found greater incidence in control AXB as compared to US-guided AXB (P=0.012). Blanco AFG,[67] found a greater incidence with RBPB as compared to IBPB. A comparison of the three techniques (SBPB, IBPB, AXB) was done by Tran DQH et al,[23] and found a greater incidence of the complication with AXB.

(c) Tingling/Numbness: Numbness/tingling is lost, reduced, or abnormal sensations in which either the sensation of the body part is lost or a person feels a sensation of pins-and-needles/prickling. It is usually a temporary sensation that returns to normal after sometimes.

We have evaluated the incidence of tingling/numbness following BPB and found that only four studies,[17,25,27,50]have reported this complication.Dhir and Ganapathy,[17] found tingling and numbness with the IBPB technique. In Parrington SJ et al study of the SBPB, a greater incidence of tingling and numbness was noted in the group in which dexamethasone was added.[25] Thomas LC found greater chances of numbness with the US-ISBPB as compared to the NS-ISBPB.[27] Kim et al found equal incidence with the ISBPN and SBPB techniques.[50]

Motor weakness: Two studies,[27,29] have found motor weakness as their complication. Thomas LC et al,[27] found more weakness with the US-ISBPB (2%) as compared to the NS-ISBPB (0%). Subramanyam R et al,[29] have reported more weakness with the medial approach (8%) as compared to the lateral approach (6%) of SBPB.

(2) Respiratory complications: A total of 23 studies,[6,20,21,22,28,30,35,43,44,46,47,48,49,50,51,53,57,64,65]reported respiratory-related complications.Among them, the most common ones are HDP (n=19), followed by pneumothorax (n=3), any other respiratory complications.

(a) Hemidiaphragmatic paralysis (HDP): HDP occurs due to blocking of ipsilateral phrenic nerve blocks which decreases the pulmonary functions of the patient.[94] In the case of surgery of the shoulder, the incidence of HDP is reported to be 1 per 2069 (0.048%).[95]We found that 19 studies reported the complication of HDP in our systematic review. Among these 19 studies, most of them belong to the ISBPB technique. According to Urmey WF et al, ISBPB is found to be associated with a 100% incidence of HDP and 25-32% reduction in the spirometric measures of the pulmonary function,[94] which restricts the use of this technique among respiratory insufficiency patients. The first case of HDP following ISBPB was reported by Bashein et al. in 1985.[96]

A systematic review conducted by Park SK et al commented that the occurrence of HDP because of PNP is an integral complication of ISBPB, its incidences associated with SBPB cannot be neglected.[85] Another systematic review conducted by Schubert AK et al found that the patients with SBPB had a significantly lower incidence of HDP than the ISBPB (42.60 versus 78.75%).[93] This holds true with our review also as we foundthat eight studies,[21,28,30,44,48,49,51,65] have reported the complication of HDP with ISBPB approach. Among these, two RCTs,[21,48] have divided the ISBPB patients into 2 groups: Ultrasound group (US) and neural stimulation (NS) and in

both of these, greater incidence of HDP was seen with NS group as compared to US group.

Many studies have tried to alter the volume of LA and found the effect on the incidence of complications. Lee JH et al have compared the effects of 5ml and 10ml LA on complications and found that 5 ml LA showed a lesser incidence of HDP (33%) to 10ml (60%).[28] Similarly, Stundner O et al found a lesser incidence of HDP with 5 ml group (27%) when compared with 20ml group (53%),[49] whereas, Sinha SK et al concluded that decreasing the volume from20 to 10 mL did not reduce the incidence of HDP.[30] Palhais A et al,[44] (21% vs 90%), Ayyanagouda B et al,[65] (17% vs 46%), and Albrecht E et al,[51] (15% vs 41%) have compared between the extrafascial and intrafascial approaches respectively and both of them were in favor that the extrafascial injection reduces the incidence of HDP.

Three studies have reported the complication of HDP with SBPB approach.[6,22,53] Renes found a lesser incidence with the US group as compared to the NS-SBPB group.[22] When the SBPB and ISBPB were compared, four studies,[46,47,50,57] have depicted higher incidence of HDP in the ISBPB technique and only Petrar has shown the lesser incidence with the ISBPB technique.[43] When the SBPB was compared with the IBPB,[20] and the CBPB,[64]a greater incidence was seen with the SBPB in both studies. Owing to the serious respiratory complications associated with ISBPB technique, it should be avoided in patients with respiratory insufficiency.

(b) Pneumothorax: Pneumothorax is a collapsed lung in which air leaks into the space present between the lungs and the chest wall.The onset of clinical manifestations usually takes time (up to 24 hours). The prevalence of pneumothorax after the SBPB ranges from 0.5 to 6%.[97] Its association with BPB administration is due to the positioning of the apex of the lung which is medial and posterior to the brachial plexus.

Three studies related to the SBPB technique reported the complication of pneumothorax.[11,24,70]Pneumothorax is a very dreaded complication that is most commonly specific to the SBPB technique.[3] Yang CW et al found a greater incidence of pneumothorax with the SBPB as compared to the IBPB.[24]Shi-ping Luh found evidence of pneumothorax in 25% of patients after the SBPB technique by using X-rays.[98]Even, our review found a greater incidence of pneumothorax with the SBPB technique and more specifically SBPB technique with neural stimulation as compared to the US-guided SBPB,[41] as the use of US have reduced the incidence of this complication to a great extent. Singh and Singham found a greater incidence with the control group as compared to clonidine and dexmedetomidine groups with SBPB technique.[70]

(c) Other respiratory complications: Dyspnea was seen in six RCTs.[24,38,43,46,50,58] Respiratory complications are also found higher with the ISBPB technique (n=5). Respiratory depression and reduce ventilator function were seen in Renes SH et al,[21] and Behr et al,[31] studies with ISBPB. Riazi S et al,[16] found lower incidence of respiratory distress with low-volume LA (5ml) as compared to the high volume (20ml) with the US-guided ISBPB technique. Dyspnea and pulmonary embolism in Bjørnholdt KT et al with the ISBPB technique.[38] Shortness of breath was seen in Rettig HC et al,[10] with SBPB and IBPB technique respectively. Deep breathing was observed in Sivashanmugam T et al study with the SBPB technique.[64] Yang CW et al,[24] found a greater incidence of dyspnea with the SBPB technique as compared to the IBPB. Petrar SD et al,[43] and Kim BG et al,[50] compared the SBPB and the ISBPB techniques but found contrasting results. The former found a lesser incidence of dyspnea with the ISBPB technique and the latter found with the SBPB technique.

(3) Cardiac disorders: Thirteen studies reported cardiac complications, of which eleven studies,[14,40,56,75,76,77,55,59,60,61,62] demonstrated hypotensive and bradycardiac events and two

studies showed tachycardia/sinus tachycardia with ISBPB and SBPB technique respectively.[68,72] We found that among thirteen studies, eight are related to the SBPB technique only.
(a) Hypotension and bradycardiac events (HBE): It is defined as a decrease in heart rate of more than 30/min in less than 5 minutes a decrease in systolic blood pressure of more than 30 mm Hg in less than 5 minutes. The possible etiology responsible for HBE are carotid sinus hypersensitivity, Bezold-Jarisch reflex, orthostatic hypotension, venous air embolism, LA toxicity or epidural/subarachnoid spread of LA.[99]

Eleven studies reported the occurrence of HBE following BPB.[14,40,56,75,76,77,55,59,60,61,62] Pippa P et al,[14] found a greater incidence in the group receiving a lesser volume of LA with the ISBPB technique**.** Ryu T et al,[40] found a greater incidence with the ISBPB group (12.8%) when compared with the SBPB (4.3%). Hong B et al,[55] also found the complication of bradycardia with BPB. Hamed MA et al,[56] Sinha,[59] Dharmarao PS et al,[60] Mangal V et al,[61] Elyazed MAM et al,[62] Sachev S et al,[75] Singh N et al,[76] and Lotfy ME et al,[77]found incidence of bradycardia and hypotension more in the group receiving dexmedetomidine as compared to the control group,[61,75] or other adjuncts such as dexamethasone,[76] fentanyl,[56,60,77] MgSO4,[62] and clonidine,[70] with SBPB technique. Sinha C et al found more incidence with the group receiving a higher dose of dexmedetomidine with SBPB technique.[59]
(4) Hoarseness: Hoarseness is a rare complication of nerve block caused due to the blockade of the recurrent laryngeal nerve (RLN). The blockade also results in RLN palsy. In the present systematic review, eight studies,[16,40,44,46,50,58,65,69] have reported hoarseness as their complication and one study reported laryngeal nerve block,[31] with the use of ISBPB technique). Among the eight studies, three of them related to only the ISBPB technique. Riazi S et al found a greater incidence with high volume (20ml) LA group as compared to low-volume LA group of the ISBPB technique.[16] Palhais A et al,[44] (35% and 5%) and Ayyanagouda B et al,[65] (31% and

3.4%) found a lesser incidence of hoarseness with extrafascial group as compared to intrafascial group of ISBPB technique respectively. Five studies reported the complication while comparing two techniques. The incidence of the RLN block during the supraclavicular approach is seen in only 1.3% of patients.[100]With regard to hoarseness, Schubert AK et al found no significant difference between SBPB and ISBPB,[93] whereas, Ryu T et al,[40] Kim et al,[50] and Singh and Singham,[69] found higher incidence with ISBPB technique (10.6%, 1%, 17.8%) as compared to SBPB technique (4.3%. 0% and 0%) respectively, whereas, Wiesmann T et al,[46] found equal incidence after one week when ISBPB and SBPB were compared. Auyong DB et al compared ISBPB, SBPB, and suprascapular techniques and found a greater incidence with ISBPB technique (22%).[58]

(5) Phrenic nerve palsy: An inevitable consequence of the ISBPB technique is PNP which sometimes results in HDP and restricts the use of this technique in patients with respiratory difficulties. The high occurrence of PNP with this technique is because of the close proximity of the phrenic nerve to the site of injection of the ISBPB technique. According to the data from the case series, the incidence of PNP after the ISBPB technique ranges from 1 in 2,000 up to 1 in 100.[95]

In our review, we found that PNP was reported by four studies,[14,37,64,69] of which three studies,[14,37,69] found higher incidence with the ISBPB technique. Pippa P et al found a greater incidence in the group receiving a lesser volume of LA (P=0.002) with the ISBPB technique.[14] Bharti N et al,[37] and Singh and Singham,[69] found a greater incidence with the ISBPB technique when compared with the SBPB and SBPB, IBPB respectively. Sivashanmugam T et al found a greater incidence with the SBPB technique (45%) as compared to the CBPB (5%).[64] A systematic review conducted by El-Boghdadly K et al concluded that "the safest option to avoid phrenic nerve block would be to avoid performing an interscalene block" altogether".[101] The potential cause of PNP is direct damage of the phrenic nerve, intraneural injection, deposition of LA to the phrenic nerve (transient PNP). The occurrence of PNP

after ISBPB was seen in various case series published in the literature.[102,103,104] But none of the studies have reported the complication with US-ISBPB as the US helps in the visibility of the nerve. The mechanism of PNP may be attributed to the chemical, ischemic or mechanical trauma caused by LA, or its needle.

(6) Other complications: Patel MA et al in their study reported visual impairment, tinnitus, and muscle twitching with the ISBPB technique.[72] Urinary retention was also reported with the ISBPB technique by Kaya M et al.[33]

(7) Complications related to LA toxicity: LA toxicity is a well-known complication of anesthesia-related procedures. The chances of this toxicity is greater with brachial plexus anesthesia as compared to others because a larger dose of LA is required in this technique and the injection site is in close proximity with the large blood vessels of the head, neck, and axillary regions. When administered in the recommended concentrations and correctly, LA procedures are safe. Toxicity occurs due to inadvertent injection of the LA to the blood vessels and absorption of the LA from the peripheral sites, administration of high concentration of LA, or intraneural injection. The complications associated with LA are:

(a) Vascular puncture: Vascular puncture refers to the injury of blood vessels either through crushing, stretching, or tearing of the blood vessels due to the needle. It is determined by the presence of frank blood in the hub of the needle or aspiration of blood when the needle was attached to the tubing and a syringe. Twenty studies,[7,8,9,10,11,12,18,20,23,24,25,26,31,32,34,35,39,52,54,67,74] measured the incidence of vascular punctures. March X et al,[9] Serradell A et al,[8] Liu FC et al,[11] Gianesello L et al,[26] Bernucc F et al,[32] and Saracoglu S et al,[34] reported vascular puncture with AXB technique. Deleuze A et al,[7] De Jose Maria B et al,[18] and Bravo D et al,[54] reported the incidence with the IBPB technique. Oztur NK et al,[52] also reported the

complication but with the coracoid approach IBPB technique. Behr A et al reported with the ISBPB technique.[31] Singh S et al,[39] and Arab SA et al,[35] reported with the SBPB technique but Singh S et al with NS-SBPB technique.[39] Heid FM et al,[12] (IBPB and AXB), Tran DQH et al,[23] (IBPB, SBPB, and AXB), and Koscielniak-Nielsen JZ et al,[20] (SBPB and IBPB) reported equal incidence of the vascular puncture in groups but Yang CW et al,[24] reported more incidence with SBPB as compared to IBPB and Blanco AFG et al,[67] reported more incidence with IBPB as compared with RBPB. Luo Q et al reported more incidence with CBPB as compared to the SBPB technique.[74] Blood aspiration during block was reported in the Rettig HC et al with IBPB technique.[10]

(b) Postoperative nausea and vomiting (PONV): The administration of LA may manifest as nausea and vomiting in some patients. It was reported in 15 studies.[10,25,31,33,42,55,56,57,58,60,62,66,72,77,78] Parrington SJ et al,[25] Kooloth RA et al,[42] Kaur S et al,[66] reported incidence of PONV in low volume LA group, ropivacaine group and ketamine group (2 $mg.kg^{-1}$ ketamine with LA) with SBPB technique respectively. Hamed MA et al,[56] Dharmarao PS et al,[60] Elyazed MAM et al,[62] and Lotfy ME et al,[77] with SBPB technique Youssef MY et al,[78] reported with the SBPB technique. Rettig HC et al,[10] with the IBPB group. Behr et al reported with more incidence with intramuscular buprenorphine the ISBPB group.[31]. Kaya M et al,[33] Auyong DB et al,[58] and Patel MA et al,[72] reported more incidence of PONV with the ISBPB technique. Hong B et al,[55] reported more incidence with the midazolam group as compared to the dexmedetomidine group. Aliste J et al,[57] found equal incidence with ISBPB and SBPB

(c) Transient burning pain and bruising at the injection site: Burning pain was reported in two studies,[29,38] with SBPB and ISBPB techniques respectively, tourniquet pain,[11] axillary pain,[15] with AXB techniques. Bruising was reported by Chan VWS et al,[15] Parrington SJ et al,[25] and Subramanyam R et al.[29] Subramanyam R et al reported the incidence of bruising

in low volume LA group and lateral approach with SBPB technique respectively.[29]

(d) Other complications: Hematoma was reported in three studies,[11,38,66]with SBPB, ISBPB, and AXB techniques respectively. The intravascular injection was reported only in one RCT,[41] constipation by Patel MA et al,[72] pruritis at the site of injection by Patel MA et al,[72] and Lofty ME et al,[77] with ISBPB and SBPB techniques respectively. Hallucination and nystagmus by Kaur S et al,[66] dry mouth by Hong B et al,[55] dizziness by Hong B et al,[55] and Bjørnholdt KT et al,[38] the headache was reported by Hong B et al,[55] and Patel MA et al,[72] dysphonia was reported by Pippa P et al.[14]

In the present systematic review, we found that although ISBPB is the most common technique of anesthesia and pain management for the procedures involving the upper limb, it constitutes several inevitable consequences such as the occurrence of Horner syndrome, HDP, PNP, Hoarseness, respiratory complications, and PONV. Owing to the highest rates of complications associated with the ISBPB technique, alternate blocks should be searched. Even Guo C et al in their systematic review concluded that US-guided SBPB could become a feasible alternative to ISBPB in shoulder surgery.[105]

Limitations

Although we performed an extensive literature search, several pitfalls do exist as we have only included the RCTs that were published in the English language only. Secondly, we have only included one type of study design (RCT). In our review, most of the RCTs have a small sample size (<60 per group) and the number of RCTs constituting a larger sample size were very less. Some RCTs were performed by the same group of authors,[19,23,21,22,69,70] which might introduce some bias in the systematic review. Hence, the above-mentioned points should be kept in mind while performing further systematic reviews on this vital topic.